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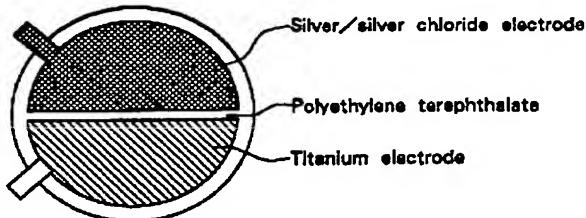
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**(54) ELECTRODE STRUCTURE FOR IONTOPHORESIS**

(57) This is an iontophoresis electrode structure comprising having both a polarization electrode and a non-polarization electrode, wherein both electrodes can be switched freely while electricity is turned on. The present electrode structure makes it possible to transfer biologically active substances and drugs into a living body in administration through the skin and the mucous

membrane in a sufficient amount and safely by employing both a polarization electrode and a non-polarization electrode as iontophoresis electrodes according to a proper switch, and can transfer biologically active substances and drugs through the skin and the mucous membrane effectively without causing irritation.

**F I G . 2**



**Description****Field of Industrial Utilization**

The present invention relates to an iontophoresis electrode structure (i. e. an electrode structure for iontophoresis) used for transferring biologically active substances or drugs into a living body in the field of medical treatment.

**Technical Background**

It has a lot of advantages including the duration of concentration in blood, the reduction of side effects to the digestive organs and the simplicity of administration to allow biologically active substances and drugs to be absorbed through the skin or the mucous membrane. However, since substance permeability through the skin is low, there has been a limit to biologically active substances and drugs capable of being transferred in a sufficient amount into a living body. Besides, it has been difficult to transfer biologically active substances having high molecular weight and drugs through a mucous membrane.

Recently, physical acceleration methods utilizing phonophoresis and iontophoresis have been studied. Of them, iontophoresis is a method of allowing ionized biologically active substances and drugs by an electric current to be absorbed through the skin or the mucous membrane and has been studied as an administration method instead of injections. Generally, as electrodes for iontophoresis have been employed polarization electrodes of platinum, titanium, carbon and the like and non-polarization electrodes of silver/silver chloride and the like.

However, in the case of employing such electrodes singly, it has not been possible to transfer biologically active substances and drugs in a sufficient amount into a living body by iontophoresis.

It is the object of the present invention to provide an electrode structure which can transfer biologically active substances and drugs into a living body effectively causing no irritation through the skin or the mucous membrane, which has been difficult according to conventional iontophoresis techniques, and also can transfer (namely, transport) biologically active substances and drugs into a living body in a sufficient amount and safely.

**Disclosure of the Invention**

The present invention provides an iontophoresis electrode structure having both a polarization electrode and a non-polarization electrode on the conducting element side, wherein both electrodes can be switched freely while electricity is turned on.

As described above, the electrode structure of the present invention has both a polarization electrode and

a non-polarization electrode and is composed so that both electrodes can be switched freely while electricity is turned on. As materials for a polarization electrode constituting the electrode structure on the conducting element side are employed titanium, aluminum, iron, platinum, alloys thereof and carbon, and as materials for a non-polarization electrode are employed silver, silver chloride, copper chloride, or materials based thereupon, for example, silver/silver chloride (silver with silver chloride adhered thereto or mixtures of both) and copper/copper chloride (copper with copper chloride adhered thereto or mixtures of both); however, they are not limited to them.

A preferred embodiment of this electrode structure is composed of a polarization electrode and a non-polarization electrode formed integrally with an electrically insulating layer (for example, a thin layer) provided between both. This electrode structure is composed, for example, as shown in Fig. 2; however, it only exemplifies one embodiment and it goes without saying that it is not limited thereto. As shown in Fig. 2, the electrode structure of the present invention is composed of a polarization electrode of titanium and alloys thereof, aluminum and alloys thereof, iron and alloys thereof and carbon and a non-polarization electrode of silver, copper, silver chloride, copper chloride, or materials based thereupon, for example, silver/silver chloride (silver with silver chloride adhered thereto or mixtures of both) and copper/copper chloride (copper with copper chloride adhered thereto or mixtures of both) with an electrical insulating material, for example, polyethylene terephthalate, polyethylene, polypropylene, polyvinylidene chloride, vinyl acetate copolymer, vinyl acetate/vinyl chloride copolymer, polyamide and cellophane provided between both.

In the electrode structure of the present invention, the polarization electrode and the non-polarization electrode are formed into a semicircular form respectively according to the circular sheet-like form in the example of Fig. 2; however, they are not limited to this embodiment but can be formed into a quadrangle, a pentagon or other proper forms with a proper thickness. In addition, the thickness and the size as a whole of the present electrode structure are selected properly according to the size and the form of diffusion cells in an iontophoresis device.

Moreover, for example, as shown in Fig. 1, in the electrode structure of the present invention, both the polarization electrode and the non-polarization electrode are connected to the cathode side of a power source device in an iontophoresis device on the conducting element side, and can be switched freely according to the switching operation of the power source device. Fig. 1 shows an embodiment in the case of administering minus-charged biologically active substances or drugs. In contrast, in the case of administering plus-charged biologically active substances or drugs, the switching device in the iontophoresis power

source device is set on the anode side (plus pole side), and the electrode on the conducting element side is connected thereto. In this case, the electrode on the non-conducting element side is connected to the cathode side (minus pole side) in the iontophoresis power source device.

In the case of administering biologically active substances or drugs into a living body according to iontophoresis, it is a novel technique to turn on electricity by employing an electrode structure comprising two kinds of electrodes as an electrode on the conducting element side like the present invention. The present invention has made it possible to transfer (namely, transport) biologically active substances or drugs into a living body in a sufficient amount and safely in administering biologically active substances or drugs through the skin or the mucous membrane.

In addition, as the electrode on the non-conducting element side, namely the anode side in iontophoresis employing the electrode structure on the conducting element side of the present invention is employed a polarization electrode or a non-polarization electrode. As materials for a polarization electrode are employed, for example, platinum, titanium, aluminum, iron, alloys thereof and carbon, and as materials for a non-polarization electrode are exemplified silver, copper and zinc. As a particularly preferable combination of an electrode on the conducting element side and an electrode on the non-conducting element side can be mentioned one wherein the electrode on the conducting element side is an electrode structure comprising titanium and silver/silver chloride, and the electrode on the non-conducting element side is silver.

In the case of administering plus-charged biologically active substances or drugs, the drugs are contained on the anode side and an electrode structure having both a polarization electrode and a non-polarization electrode on the anode side is employed. As the polarization electrode in this case is employed titanium, aluminum, iron, platinum, an alloy thereof or carbon, and as the non-polarization electrode is employed silver, copper or an alloy thereof. As a preferable combination can be mentioned titanium and silver, and carbon and silver. Moreover, in the case of administering minus-charged biologically active substances or drugs, the drugs are contained on the cathode side and an electrode structure having both a polarization electrode and a non-polarization electrode on the cathode side is employed. As the polarization electrode in this case is employed titanium, aluminum, iron, platinum, an alloy thereof or carbon, and as the non-polarization electrode is employed an electrode based on silver chloride and copper chloride. As a preferable combination can be mentioned titanium and silver/silver chloride, and carbon and silver/silver chloride.

The biologically active substances or drugs employed and used in the practice of the present invention are not particularly limited and include, for example,

5 anaesthetic agents, analgesic agents, anorexic agents, vermicides, antasthmatics, anticonvulsion agents, anti-diarrheal agents, antimigraine agents, anti-motion-sickness agents, antivomiting agents, antitumor agents, anti-Parkinson's disease agents, antipruritics, antipyretic agents, sympathetic agents, xanthine derivatives, cardiovascular agents such as calcium transport route blocking agents, beta-blocking agents, antiarrhythmic agents, hypotensive agents, diuretic agents, vasodilators including the whole body, the coronal blood vessel, 10 the peripheral blood vessel and the cerebral blood vessel, central nervous system excitatory state agents, drugs for coughs and colds, decongestants, diagnosis agents, hormones, sleeping drugs, immunosuppressants, muscle relaxants, parasympathetic suppressants, parasympathetic agents, nervous excitatory state agents, sedatives, tranquilizers, anti-inflammatory agents, antiarthritis agents, antispasmodics, antidepressant agents, drugs for neurotic diseases, drugs for anxiety neurosis, anaesthetic antagonists, carcinostatics, 15 immunosuppressants, antivirus agents, antibiotics, anoretics, antiemetics, anticholine agents, antihistamine agents, hormone drugs, contraceptives and anti-thrombophilia agents; however, they are not limited to them.

20 Specific examples of the biologically active substances or drugs include insulin of peptides, calcitonins, calcitonin-connected gene peptides, vasopressin, desmopressin, protirelin (TRH), adrenocorticotrophic hormone (ACTH), luteinizing hormone-releasing factor (LH-RH), growth hormone-releasing factor (GRH), nerve growth factor (NGF) and other releasing factors, 25 angiotensin, parathyroid hormone (PTH), thyroid-stimulating hormone (TSH, thyrotropin), follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, serum gonadotropin, placental gonadotropin, 30 hormone (HCG), pituitary gonadotropin hormone (HMG), growth hormone, somatostatin, somatomedin, glucagon, oxytocin, gastrins, secretin, endorphin, enkephalin, endoserine, cholestquinin, neurotensin, interferon, interleukin, transferrin, erythropoietin, superoxide dismutase (SOD), granulocyte stimulating factor (G-CSF), vasoactive intestinal polypeptide (VIP), muramyl dipeptide, corticotropin, urogastrone and 35 human atrial natriuretic peptide (h-ANP); however, they are not limited to them.

#### Brief Description of the Drawings

40 Fig. 1 is a schematic view showing an embodiment of an iontophoresis test device employing an iontophoresis electrode structure according to the present invention. Fig. 2 is a schematic view showing an embodiment of an iontophoresis electrode structure according to the present invention on the conducting element side. Fig. 3 is a diagram showing insulin concentration in blood after one hour in Examples of the present invention, and Fig. 4 is a diagram showing areas under the 45

time curve of insulin concentration in blood in Examples of the present invention. Fig. 5 is a diagram showing the mucous membrane permeability of insulin till three hours after in Examples of the present invention, and Fig. 6 is a diagram showing an electrode time schedule in Example 2-3 in Test Example 2.

#### Preferred Embodiments for Performing the Invention

Hereunder, the present invention will be described in detail. First of all, the outlines of Test Examples (Examples) will be described, and then these Test Examples (Examples) will be described more specifically. As a test device for use was employed an iontophoresis device as shown in Fig. 1.

#### Test Example 1

In Test Example 1, the back of a rat (a SD-strain rat: 250 g) was fixed, a diffusion cell was set thereon, and an insulin solution was administered thereto (amount of administration: 25 IU). On the non-conducting element side directly connected to said back part, a sodium chloride-containing PVA gel formed integrally together with an electrode was employed. To an iontophoresis power source device as shown in Fig. 1, an electrode on the conducting element side was connected to the cathode, and an electrode on the non-conducting element side was connected to the anode.

As the electrode on the conducting element side (cathode) in Examples was employed an electrode structure comprising a titanium electrode and a silver/silver chloride electrode with polyethylene terephthalate provided between both according to the constitution as shown in Fig. 2, and as the electrode on the non-conducting element side (anode) was employed a silver electrode. On the other hand, as both the electrode on the conducting element side (cathode) and the electrode on the non-conducting element side (anode) in Comparative Examples were employed those to be described below.

In the present test, blood was collected from the rat to the fourth hour with time after turning on electricity, insulin concentration in blood was measured, and Example 1-1, Comparative Example 1-1, Comparative Example 1-2 and Comparative Example 1-3 were conducted.

#### Example 1

In Example 1-1, electricity was turned on at a voltage of 12 V for 15 minutes after the start of the test, employing a titanium electrode (namely, a titanium electrode of an electrode structure comprising a titanium electrode and silver/silver chloride) on the conducting element side and a silver electrode on the non-conducting element side. Thereafter, electricity was turned on at a voltage of 6 V for 45 minutes, employing a silver/silver

chloride electrode (namely, a silver/silver chloride electrode of an electrode structure comprising a titanium electrode and silver/silver chloride) on the conducting element side and the same silver electrode on the non-conducting element side. In this case, the insulin concentration in blood after one hour in total was about 1000  $\mu$  IU/ml. The insulin concentration in blood - area under the time curve  $AUC_0 \rightarrow 4h$  to the fourth hour was about 1.3 IU/ml min (see Fig. 3 and Fig. 4). No irritation was observed on the skin (see Table 1).

#### Comparative Example 1

On the other hand, a silver/silver chloride electrode was employed on the conducting element side and a silver electrode was employed on the non-conducting element side in Comparative Example 1-1; platinum electrodes were employed on both the conducting element side and the non-conducting element side in Comparative Example 1-2; and titanium electrodes were employed on both the conducting element side and the non-conducting element side in Comparative Example 1-3.

In the case of employing a silver/silver chloride electrode on the conducting element side and a silver electrode on the non-conducting element side as in Comparative Example 1-1 and in the case of employing platinum electrodes on both the conducting element side and the non-conducting element side as in Comparative Example 1-2, insulin hardly permeated the skin for one hour after the start of the test, and insulin in the collected blood could not be measured. In the case of turning on electricity by only titanium electrodes on both the conducting element side and the non-conducting element side as in Comparative Example 1-3, the insulin concentration in blood one hour after the start of the test was about 500  $\mu$  IU/ml, and the insulin concentration in blood - area under the time curve ( $AUC_0 \rightarrow 4h$ ) to the fourth hour was about 0.5 IU/ml min. However, as a result of observing the skin after the completion of the test, stigmas recognized to be irritation were observed.

As shown above, it was possible to transfer insulin through the skin safely by employing the electrode structure comprising both a polarization electrode and a non-polarization electrode as in Example 1-1 of the present invention and employing the polarization electrode and the non-polarization electrode according to a switch with time. On the other hand, in the case of employing a non-polarization electrode or a polarization electrode singly as in Comparative Example 1-1, Comparative Example 1-2 and Comparative Example 1-3, it was difficult to transfer insulin into a living body without causing irritation on the skin.

#### Test Example 2

In Test Example 2, the cheek bags of a hamster were extirpated, and the corneum of the cheek bags

was removed by means of a cellophane tape, which was used as a model film of the transmucosa. The mucous membrane was set in a diffusion cell having two chambers for a permeability test as shown in Fig. 1 as the mucous membrane, and an electrode on the donor side and an electrode on the receiver side were connected to the iontophoresis power source device as a cathode and an anode respectively. In this case, as the electrode on the conducting element side used in Examples was employed an electrode structure as shown in Fig. 2. The electrode structure is composed of a titanium electrode and a silver/silver chloride electrode with polyethylene terephthalate provided between both. On the other hand, the electrode on the conducting element side used in Comparative Examples was a single electrode without a switching device. After they were set as shown in Fig. 1, an insulin solution (insulin concentration: 60 IU) was supplied on the donor side, a phosphoric acid buffer solution was supplied on the receiver side, and Example 2-1, Example 2-2, Example 2-3, Comparative Example 2-1, Comparative Example 2-2 and Comparative Example 2-3 were conducted.

#### Example 2

First of all, in Example 2-1, electricity was turned on at a voltage of 18 V for 15 minutes after the start of the test, employing the titanium electrode in the above electrode structure on the conducting element side and a silver electrode on the non-conducting side; thereafter, the switching device of the iontophoresis power source device was changed, and electricity was turned on at a voltage of 3 V for 2 hours 45 minutes, employing the silver/silver chloride electrode in the above electrode structure on the conducting element side and the same silver electrode on the non-conducting side. In this case, 0.7 IU of insulin per 1 cm<sup>2</sup> permeated the mucous membrane, and no irritation was observed on the mucous membrane.

In Example 2-2, electricity was turned on at a voltage of 18 V for 15 minutes after the start of the test, employing the titanium electrode in the above electrode structure on the conducting element side and a silver electrode on the non-conducting element side; thereafter, the switching device of the iontophoresis power source device was worked, and electricity was turned on at a voltage of 6 V for 2 hours 45 minutes, employing the silver chloride electrode in the above electrode structure on the conducting element side and the same silver electrode on the non-conducting side. In this case, 3 IU of insulin per 1 cm<sup>2</sup> permeated the mucous membrane in 3 hours in total, and no irritation was observed on the mucous membrane.

Further in Example 2-3, electricity was turned on at a voltage of 6 V for 5 minutes after the start of the test, employing the titanium electrode in the above electrode structure on the conducting element side and a silver electrode on the non-conducting element side; thereaf-

ter, the conducting element side was switched to the silver/silver chloride electrode in the above electrode structure, and electricity was turned on at a voltage of 6 V for 10 minutes (15 minutes in total). This was deemed as one cycle, and electricity was turned on over 12 cycles in total, namely, over 3 hours in total. Fig. 6 shows an electrode time schedule in Example 2-3. In the case of Example 2-3, 5 IU of insulin permeated the mucous membrane in 3 hours in total, and no irritation was observed on the mucous membrane (see Fig. 5 and Table 2).

#### Comparative Example 2

On the other hand, a silver/silver chloride electrode was employed on the conducting element side and a silver electrode was employed on the non-conducting element side in Comparative Example 2-1, and platinum electrodes were employed as electrodes on both the conducting element side and the non-conducting element side in Comparative Example 2-2. In both cases of Comparative Example 2-1 and Comparative Example 2-2, insulin hardly permeated the mucous membrane for 3 hours.

In Comparative Example 2-3, electricity was turned on at a voltage of 18 V for 15 minutes after the start of the test and then at a voltage of 3 V for 2 hours and 45 minutes, employing titanium electrodes as electrodes on both the conducting element side and the non-conducting element side. In the case of Comparative Example 2-3, about 0.3 IU of insulin per 1 cm<sup>2</sup> permeated in 3 hours, but as a result of observing the mucous membrane after the completion of the test, irritation was observed thereon.

In the present Test Example 2, it was possible to transfer insulin through the mucous membrane without causing irritation through the mucous membrane by employing the electrode structure as employed in Example 2-1, Example 2-2 and Example 2-3. On the other hand, in the case of employing a non-polarization electrode or a polarization electrode singly as in Comparative Example 2-1, Comparative Example 2-2 and Comparative Example 2-3, it was not possible to allow insulin to permeate the mucous membrane without causing irritation on the mucous membrane. As described above, the present invention has made it possible to transfer biologically active substances and drugs into a living body through the skin and the mucous membrane, which was difficult according to prior arts, and to perform the transfer without causing irritation on the skin and the mucous membrane.

#### Functions

Polarization electrodes comprising metals such as Ti, Al and Fe generally electrolyze water when electricity is turned on and generate OH<sup>-</sup>. Thereby the dissolution of the tissue of the skin and the mucous membrane

slightly observed occurs. Substances can be transferred safely and efficiently further by performing iontophoresis administration, employing a non-polarization electrode.

Hereunder, the above Test Examples (Examples) will be described more specifically.

#### Test Example 1

The back of a rat (a SD-strain rat: 250 g) was fixed, a diffusion cell was set thereon, an insulin solution was administered thereto (amount of administration: 25 IU), and the insulin solution side was made a compartment on the conducting element side. Onto the non-conducting element side was applied a sodium chloride-containing PVA gel formed integrally together with an electrode. An electrode on the conducting element side was connected to the cathode of the iontophoresis power source device, and an electrode on the non-conducting element side was connected to the iontophoresis power source device as the anode. After electricity started to be turned on, blood was collected from the rat with time, and insulin concentration in the collected blood was measured.

After the completion of the test, the skin was observed. The electrodes with electricity turned on and the time while electricity was turned on in Comparative Example 1-1 to Comparative Example 1-3 and Example 1-1 were as described below. In addition,  $AUC_0 \rightarrow 4h$  was calculated according to the trapezoid method. The results thereof are as shown in Fig. 3, Fig. 4 and Table 1.

Table 1

Skin irritation	Presence of irritation
Example 1-1	Nil
Comparative Example 1-1	Nil
Comparative Example 1-2	Nil
Comparative Example 1-3	Observed

#### Example 1-1

Electricity was turned on at a voltage of 12 V for 15 minutes after the start of the test, employing a titanium electrode as the electrode on the conducting element side and a silver electrode as the electrode on the non-conducting element side; thereafter, electricity was turned on at a voltage of 6 V for 45 minutes, employing a silver/silver chloride electrode as the electrode on the conducting element side and a silver electrode as the electrode on the non-conducting element side.

#### Comparative Example 1-1

Electricity was turned on at a voltage of 12 V for 15 minutes after the start of the test, employing a silver/silver chloride electrode on the conducting element side and a silver electrode on the non-conducting element side; thereafter, electricity was turned on at a voltage of 3 V for 45 minutes.

#### Comparative Example 1-2

Electricity was turned on at a voltage of 12 V for 15 minutes after the start of the test, employing platinum electrodes as electrodes on both the conducting element side and the non-conducting element side; thereafter, electricity was turned on at a voltage of 3 V for 45 minutes.

#### Comparative Example 1-3

Electricity was turned on at a voltage of 12 V for 15 minutes after the start of the test, employing titanium electrodes as electrodes on both the conducting element side and the non-conducting element side; thereafter, electricity was turned on at a voltage of 3 V for 45 minutes.

#### Test Example 2

In the present Test Example, a two-chamber diffusion cell device for a permeability test as shown in Fig. 1 was employed, and the electrode on the conducting element side in Examples was employed an electrode structure as shown in Fig. 2. On the other hand, as the electrode on the conducting element side (cathode) and the electrode on the non-conducting element side (anode) in Comparative Examples were employed electrodes to be described below.

The cheek bags of a hamster (a syrian golden hamster; weight: 100 to 150 g) were extirpated, and the corneum thereof was removed by means of a cellophane tape. The film was set in the two-chamber diffusion cell for a permeability test. An insulin solution (insulin concentration: 60 IU) was applied onto the compartment on the donor side (conducting element side), and a phosphoric acid buffer solution was applied onto the compartment on the receiver side (non-conducting element side). The electrode on the donor side and the electrode on the receiver side were connected to the iontophoresis power source device as a cathode and an anode respectively. Besides, after the completion of the test, the mucous membrane was observed. The electrodes with electricity turned on and the time while electricity was turned on are as described in Example 2-1 to Example 2-3 and Comparative Example 2-1 to Comparative Example 2-3 below respectively. The results thereof are as shown in Fig. 5 and Table 2.

Table 2

Mucous membrane irritation	Presence of irritation
Example 2-1	Nil
Example 2-2	Nil
Example 2-3	Nil
Comparative Example 2-1	Nil
Comparative Example 2-2	Nil
Comparative Example 2-3	Observed

Example 2-1

Electricity was turned on at a voltage of 18 V for 15 minutes after the start of the test, employing a titanium electrode as the electrode on the conducting element side and a silver electrode as the electrode on the non-conducting element side; thereafter, electricity was turned on at a voltage of 3 V for 2 hours 45 minutes, employing a silver/silver chloride electrode as the electrode on the conducting element side and a silver electrode as the electrode on the non-conducting element side.

Example 2-2

Electricity was turned on at a voltage of 18 V for 15 minutes after the start of the test, employing a titanium electrode as the electrode on the conducting element side and a silver electrode as the electrode on the non-conducting element side; thereafter, electricity was turned on at a voltage of 6 V for 2 hours 45 minutes, employing a silver/silver chloride electrode as the electrode on the conducting element side and a silver electrode as the electrode on the non-conducting element side.

Example 2-3

Electricity was turned on at a voltage of 6 V for 5 minutes after the start of the test, employing a titanium electrode as the electrode on the conducting element side and a silver electrode as the electrode on the non-conducting element side; thereafter, electricity was turned on at a voltage of 6 V for 10 minutes, employing a silver/silver chloride electrode as the electrode on the conducting element side (15 minutes in total). This was deemed as one cycle, and electricity was turned on over 12 cycles in total, namely, over 3 hours. Fig. 6 shows an electrode time schedule in Example 2-3.

Comparative Example 2-1

Electricity was turned on at a voltage of 18 V for 15

minutes after the start of the test, employing a silver/silver chloride electrode on the conducting element side and a silver electrode on the non-conducting element side; thereafter, electricity was turned on at a voltage of 3 V for 2 hours 45 minutes.

Comparative Example 2-2

Electricity was turned on at a voltage of 18 V for 15 minutes after the start of the test, employing platinum electrodes as electrodes on both the conducting element side and the non-conducting element side; thereafter, electricity was turned on at a voltage of 3 V for 2 hours 45 minutes.

Comparative Example 2-3

Electricity was turned on at a voltage of 18 V for 15 minutes after the start of the test, employing titanium electrodes as electrodes on both the conducting element side and the non-conducting element side; thereafter, electricity was turned on at a voltage of 3 V for 2 hours 45 minutes.

Effects of the Invention

The present invention makes it possible in iontophoresis to transfer biologically active substances and drugs into a living body in administration through the skin and the mucous membrane in a sufficient amount and safely by employing an electrode structure having both a polarization electrode and a non-polarization electrode as electrodes on the conducting element side and using the polarization electrode or the non-polarization electrode according to a proper switch, and can transfer biologically active substances and drugs through the skin and the mucous membrane effectively without causing irritation.

Claims

1. An iontophoresis electrode structure comprising having both a polarization electrode and a non-polarization electrode on the conducting element side, wherein both electrodes can be switched freely while electricity is turned on.
2. An iontophoresis electrode structure as claimed in Claim 1, wherein the polarization electrode and the non-polarization electrode are formed integrally with an electric insulating material provided between both.
3. An iontophoresis electrode structure as claimed in Claim 1 or Claim 2, wherein the polarization electrode is a polarization electrode comprising a material selected from the group consisting of titanium, iron, aluminum, platinum and alloys thereof, and

carbon.

4. An iontophoresis electrode structure as claimed in Claim 1 or Claim 2, wherein the non-polarization electrode is a non-polarization electrode comprising a material selected from the group consisting of silver, copper, silver chloride, copper chloride and materials based thereon. 5
5. An iontophoresis electrode structure as claimed in Claim 1 or Claim 2, wherein the electrode structure is composed in a sheet-like form. 10

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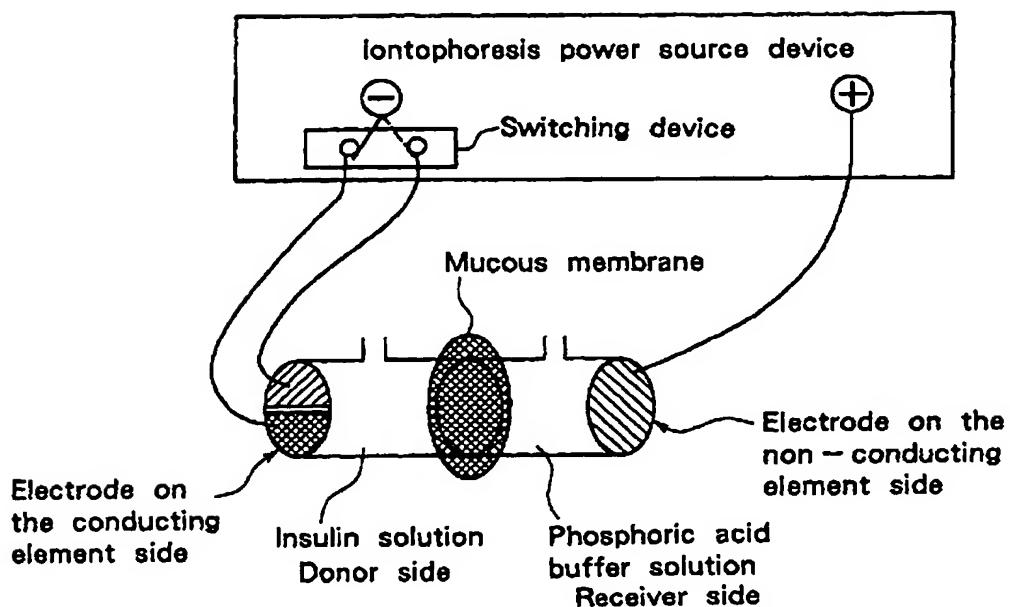
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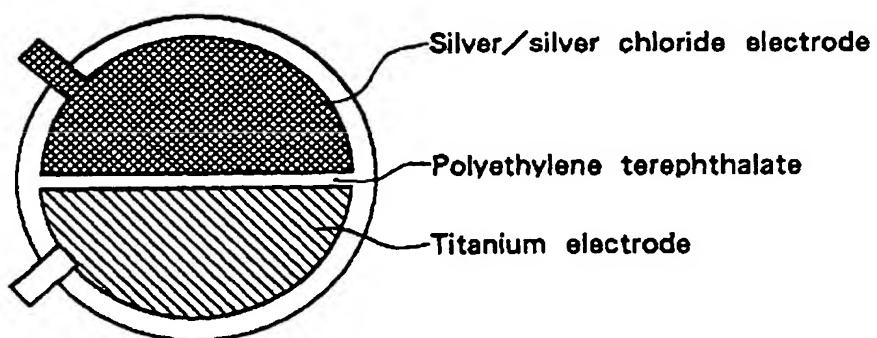
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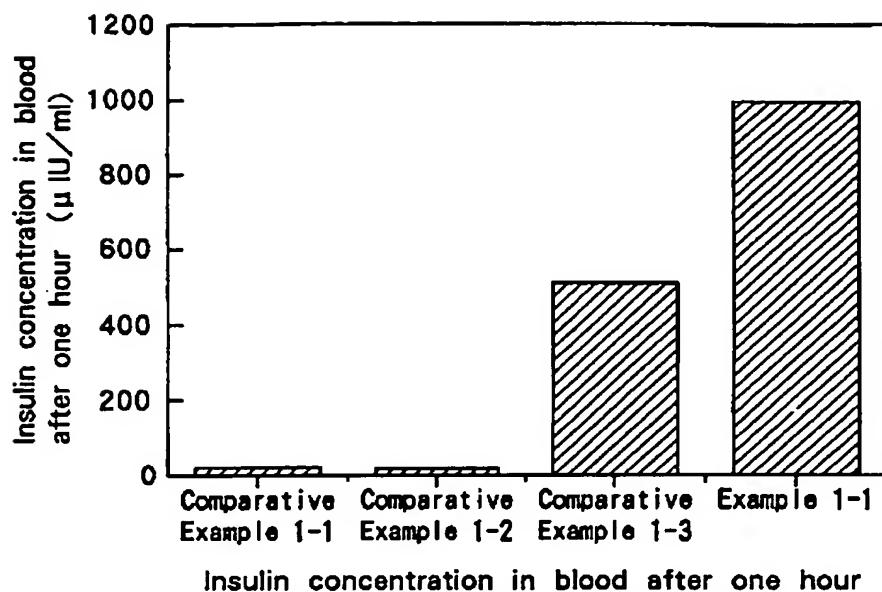
F I G . 1



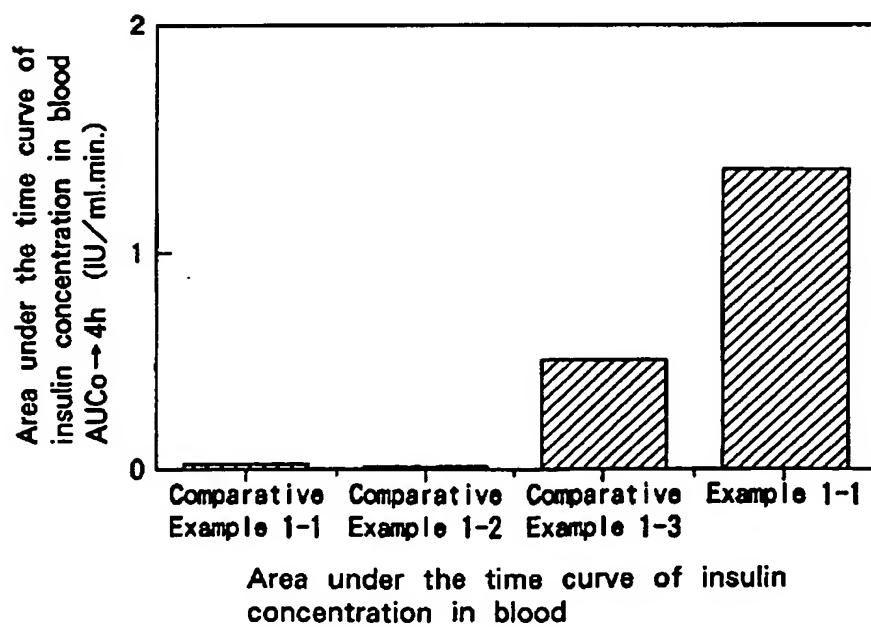
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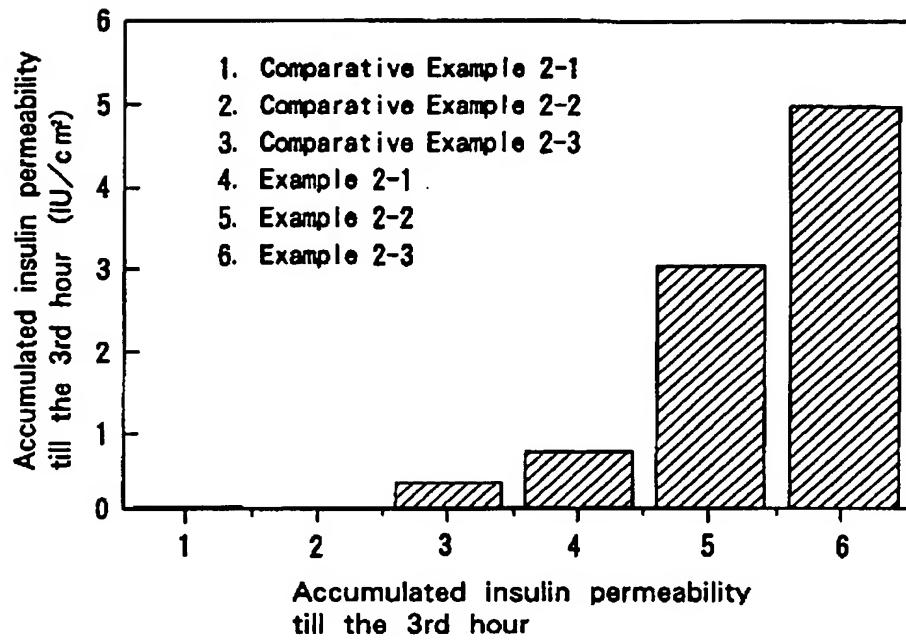
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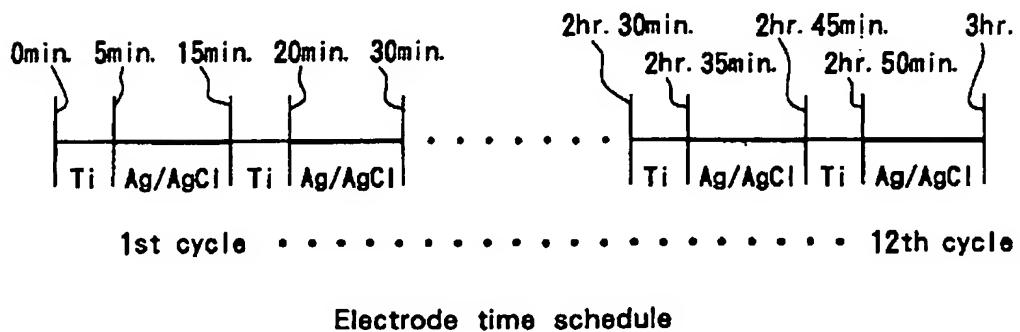
F I G . 4



F I G . 5



F I G . 6



## INTERNATIONAL SEARCH REPORT

International application No. PCT/JP95/01.619
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A. CLASSIFICATION OF SUBJECT MATTER Int. Cl <sup>6</sup> A61N1/30
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
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Minimum documentation searched (classification system followed by classification symbols)  
Int. Cl<sup>6</sup> A61N1/30

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
Jitsuyo Shinan Koho 1926 - 1995  
Kokai Jitsuyo Shinan Koho 1971 - 1995

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT
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Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JP, 6-327777, A (Gijutsu Kenkyu Kumiai Iryo Fukushi Kiki Kenkyusho), November 29, 1994 (29. 11. 94) (Family: none)	1. - 5

Further documents are listed in the continuation of Box C.

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Date of the actual completion of the international search  
November 21, 1995 (21. 11. 95)

Date of mailing of the international search report  
December 12, 1995 (12. 12. 95)

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